suggested that injections of bacterial filtrates into the eye, particularly into the conjunctival tissue, constitute a more delicate biological test for the detection of certain toxins than the tests usually employed for this purpose.

4. The experiments recorded in this paper furnish additional examples, in a comparatively new field, of the importance of toxins in explaining the pathogenic action of bacteria, and likewise emphasize the etiological significance of injuries of the covering membrane of the eye in favoring the action of toxins and of bacteria.

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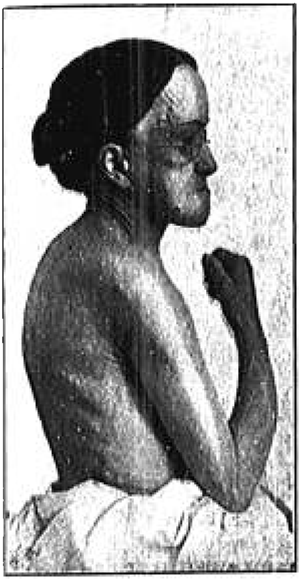
OSTEITIS DEFORMANS AND HYPEROSTOSIS CRANII. A CONTRIBUTION TO THEIR PATHOLOGY, WITH A REPORT OF CASES.

BY MORTON PRINCE, M.D.,
OF BOSTON.

THE symptomatology and general features of osteitis deformans have been so exhaustively discussed in this country within a recent period in the monographs of Elting, Wilson, and Packard, Steele and Kirkbride, that I shall limit myself in this communication to a brief description of two cases and to the question of its pathology. The last-named writers have not only contributed a valuable addition to our knowledge of the anatomical lesions, but also an important summary of the data furnished by sixty-six cases collected from the literature.

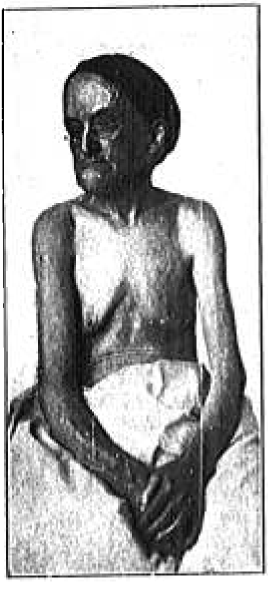
CASE I.—Mrs. M., aged forty-four years, was referred on November 1, 1901, to my clinic at the Boston City Hospital from the Eye Department, to which she had applied for impairment of vision, but the ophthalmic records note only errors of refraction. She was referred to me for certain neuralgic pains in her head. The peculiar enlargement and deformity of the cranium and jaw were noticeable and led to a careful examination of the osseous system.

FIG. 1.



CASE I. Osteitis deformans, aged 44 years, showing deformity of jaw, right forearm, kyphosis and temporal artery.

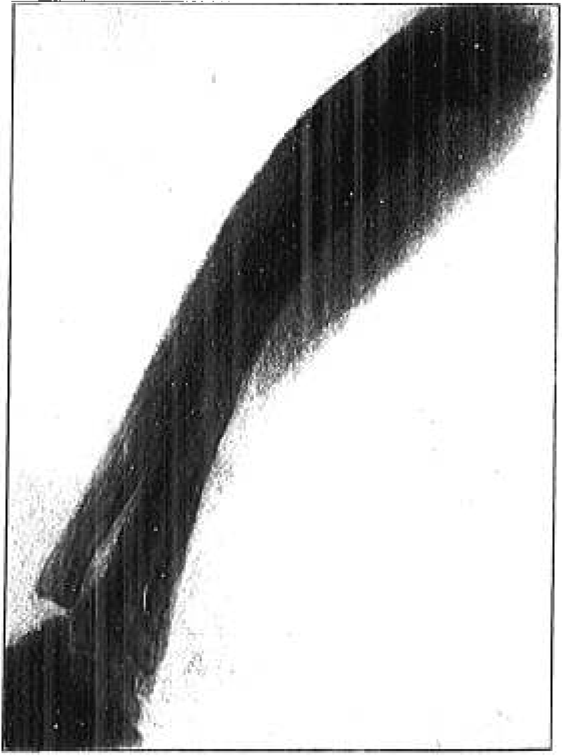
FIG. 2.



CASE I. Osteitis deformans, showing enlargement of parieto-occipital region, arterio-sclerosis, and deformity of radius, right arm.

As to her previous history and the family history, they were practically negative. There were no evidences of syphilis. She had not had a pain or an ache referable to her present condition until April, 1901, when she had some dizziness (heart?), and a month later she experienced some pain in her head. From May to October she was free from pain and all other symptoms excepting the impaired eyesight, for which she was fitted with glasses. On November 1st her symptoms were mild, and, such as they were, consisted of neuralgic pains in the head, tinnitus aurium and cardiac fluttering. Until two years ago she had never noticed any deformity of the bones—not until the curvature and enlargement of the right forearm were pointed out to her by a friend—and when first examined she was entirely uncon-

FIG. 3.

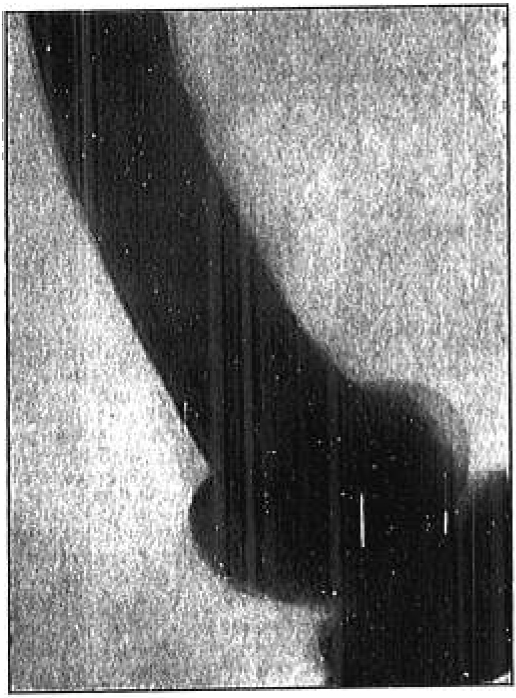


CASE I. Osteitis deformans; right radius, showing curvature.

scious of the extreme deformity of the skull that exists and of the obtrusive bending and thickening of the bones of the legs.

On first inspection, aside from the asymmetry of the skull and jaw, the most noticeable peculiarity about her is the general degeneration of her physique. She looks much older than she is; she is short of stature, bent over, and has generally small, poorly developed muscles. There is a lack of color and vascularity of the skin, which has a dried and slightly yellow appearance. Physical degeneration is stamped upon her. She looks shrunken in height and development. On her temples enlarged and tortuous atheromatous arteries stand out and strike the eye. The heart is enlarged, the apex being one inch outside

FIG. 4.



CASE I. Right femur. (The curvature and hypertrophy would be more apparent if the whole length of the bone were reproduced in the cut.)

the mammillary line, but in the fifth space, and its action is heaving. A systolic murmur is heard over the aortic valves and at the apex whither it is probably transmitted. The eyes are unusually prominent. (Figs. 1 and 2.)

Osseous System. The condition of the bones resembles in general that which has been frequently described in cases of osteitis deformans. The cranium is irregular and enlarged, although the hyperostosis is most obtrusive in the left parietal bone. The circumference of the fronto-occipital region is 61½ cm. The ramus of the jaw on the right is thickened and prominent to the eye; the spine is very slightly flexible, and has a marked kyphosis in the upper dorsal region. There is some deformity of the sternum from thickening; both clavicles are enlarged, the ribs thickened. The bones of the upper arms appear to be normal; but both radii, the right being the most affected, are thickened and curved, the bowing being outward. The last phalanges of the first and second fingers of both hands exhibit nodular thickenings and are distorted, being everted at an angle outward, giving the *impression of an osteo-arthritis.*

Coming to the lower half of the body, both femora are curved and greatly thickened, as are the tibiæ. As in the forearm, the right side is more largely affected than the left; the bones of the pelvis are also involved in the process. The photographs and skiagraphs show fairly well the conditions present. Examination of the blood failed to throw any light on the morbid process, showing simply a mild secondary anæmia.[1] Examination of the nervous system at this time was negative.

Since my last examination of this patient she entered the Massachusetts General Hospital, where she came under the observation of Dr. Fitz, who also has made a careful study of her condition. While in this hospital she developed delusions and other mental symptoms, and was removed to the Boston Insane Hospital, where she now is under the charge of Dr. Lane, who has kindly furnished me with notes of her present condition, which is that of a rather mild stupor, with some depressions and delusions.

The most interesting problems connected with this most interesting disease are its pathology and its relation to allied affections. The symptomatology has been adequately and exhaustively discussed within the limits of our present knowledge in the paper presented to this Association by Drs. Packard and Steele at the last meeting. It will be remembered that the basic and anatomical process in osteitis deformans as shown by the microscopic changes was summed up (but as I shall show incompletely) by these authors as follows:

"*a.* Absorption of the compact substance, causing enlargement and confluence of the Haversian canals.

"*b.* Formation of new bone, which runs diffusely through the affected and the adjacent healthy portions. This new bone remains uncalcified, and is in turn reabsorbed.

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[1] White count, 3800; red count, 3,768,000; hæmoglobin, 65 per cent. Differential count: polymorphonuclear neutrophiles, 66 per cent.; small lymphocytes, 26 per cent; large lymphocytes, 6 per cent.; eosinophiles, 2 per cent.

"*c.* The conversion of the medullary substance into a vascular connective tissue containing fat cells, giant cells, and leucocytes.

"*d.* As a consequence of these three processes the ordinary relations of the compact substance and medulla are destroyed. The bones become exceedingly thickened and asymmetrical, but since the new bone tissue remains uncalcified its elasticity permits of great deformity of the long bones from the weight of the body, and fractures do not occur."

This summary is incomplete in that it neglects to take into account the important fact that often *calcification does take place in the new bone*, and then a different picture is presented.

Clinically considered, the disease resembles in the peculiar enlargement and deformity of the skull what has been noted and described in hyperostosis cranii, or leontiasis ossia, and although the two diseases are regarded as distinct, it is interesting to reconsider whether, after all, hyperostosis cranii may not be an incomplete development of the same process, and, therefore, the same disease. Putnam,[1] in his exhaustive and critical paper, in 1896, has already recorded one case of my own of hyperostosis cranii. I have now to report another interesting case, which in general appearance and certain other respects bears a most striking resemblance to the case of osteitis deformans I have just reported.

CASE II.—The patient, Miss A., is sixty-three years of age, and looks about ten years older. Her general physical appearance is that of degeneration. She is short and considerably shrunken from her former height, due to the marked kyphosis in the cervico-dorsal region. The anterior borders of the ribs correspondingly approximate the pelvis. There is very marked arterio-sclerosis, which is particularly obtrusive in the temporal arteries, which stand out prominently tortuous and rigid, as in Case I. The eyes are rather prominent and the face thin. All the muscles of the body are extremely small, simulating a dystrophy. The arms, for example, would be small for a child. There are certain nervous symptoms of an atypical character. There is no paralysis, but a decided myasthenia. The gait is shuffling and unsteady, as if rather from a lack of confidence than from any real ataxia; deep reflexes are normal. There are no sensory disturbances. Her ideation is not normal, and yet it is not easy to give it a definite characterization. There is a tendency to fads, eccentricities, and fixed ideas. For example, she will not shake hands with anybody, on the theory that germs of disease are conveyed in that way. She is extremely difficult to influence, owing to her ideas, and she lives a life of exclusiveness; in other words, she presents what one meets with in arterio-sclerosis at times. The cranium is conspicuously enlarged, the hypertrophy of the bone being the most marked on either side in the parieto-occipital region. The frontal bone is also prominent. The head gives the impression of being too large for the face. The patient is not aware of this enlargement of her head, but I am told that it has existed for some twenty years(?). The cervico-dorsal spine is rigid, as if ankylosed. The long bones are small, as if atrophic, like the muscles, but not bent abnormally. She is free from pain and other symptoms, excepting that she is slightly deaf. The eyes were not examined. It was difficult to obtain a complete examination, which was, therefore, somewhat limited, and not as thorough as could be wished.

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[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1896.

Whether such a case as this should be classified with hyperostosis' and not as an incomplete case of osteitis deformans, is difficult to answer in the absence of any fundamental criterion. The hypertrophy of the cranium without involvement of the long bones gives a striking resemblance to hyperostosis cranii, while the kyphosis and apparent ankylosis of the spine, giving the effect of a spondylitis deformans, the generally impaired nutrition, and the arterio-sclerosis, are suggestive at least of osteitis deformans.

Putnam, in his excellent monograph on hyperostosis cranii, somewhat summarily dismisses the question of the possible identity of this disease with Paget's, as do almost all writers on Paget's disease, on the ground that the latter affects the long bones and is a disease of advanced age. It seems to me that each succeeding writer passes over this question somewhat cursorily, without due consideration, as if the idea of non-identity were handed down as a transmittendum from the earlier writers.

In addition to Putnam's collection of fourteen cases of hyperostosis cranii, I have been able to find six others reported to date by Horsley,[1] Ellis,[2] Priestly,[3] Sattler,[4] Parker,[5] and Roberts,[6] respectively. These, with the above case of my own, make twenty-one.[7]

Of these twenty-one cases ten apparently began after thirty years of age, and four after forty; and, conversely, of Packard, Steele and Kirkbride's collection of sixty-six cases of osteitis deformans, in eleven the disease began before the age of forty. Moizard and Bourges report a case in which the onset occurred at twenty-one years, and Blanc reports one beginning at seventeen years, but in this last the accuracy of the diagnosis is not above suspicion. At any rate, considering the small number of cases of hyperostosis cranii on record, the age limit seems to be hardly a sufficient criterion.

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[1] Practitioner, London, 1895, iv. 12-25.

[2] Archives of Ophthalmology, 1899, xxviii. 4.

[3] Quarterly Medical Journal, Sheffield, 1898, vii. 154.

[4] Cincinnati Lancet-Clinic, 1897, and Transactions of the American Ophthalmological Society, 1900. In the second paper the autopsy is reported.

[5] Annals of Surgery, 1894.

[6] Ibid., 1896.

[7] Ten other cases described under this title are to be found in the literature, but with insufficient evidence of the nature of the disease. Under a hyperostosis cranii a variety of diseases has been included from mere local tumors to a diffused condition, which later observation has shown to be osteitis deformans or some other process. In the absence of any definite criterion, I have been perhaps somewhat arbitrary in the exclusion of questionable cases. Perhaps future investigations may show that some of these may be varieties of the disease in question, but at present it would seem to be wiser to limit our study to typical cases. I, therefore, only include those cases in which the bones of the head have been more or less diffusely affected.

As to the non-involvement of the *long bones*, Bowlby and Edmunds have each reported a case claiming to be osteitis deformans in which only one long bone was affected, and Hutchinson a case in which only two long bones were affected. In Bowlby's case the histological examination showed changes resembling those described by Paget, so that if the disease may be limited to one bone it is logically possible that it may be limited to the cranium, which is so often and early affected.

It has been argued that a distinction between the two diseases is to be found in the hypertrophy of the malar bones in hyperostosis cranii giving the leonine appearance (leontiasis ossia), but this is not always found in this disease, and, conversely, I find that a careful examination of recorded cases shows that the bones of the upper face are not always unaffected in Paget's disease. For example, besides minor hypertrophic changes, like hypertrophy of the superior alveolar border found by Joncheray[1] and Meunier,[2] and of the inferior orbital arches in two cases recorded by Lunn,[3] Meunier found hypertrophy of the malar bones giving the appearance of leontiasis ossia in a typical case of osteitis deformans. Likewise, Gilles de la Tourette and Magdalaine[4] report a similar hypertrophy of the malar bones, as does Pic;[5] so that the presence or absence of this particular hypertrophy would not seem to have the importance ascribed to it.

From the point of view of pathological anatomy the differentiation of the two affections is equally difficult. In hyperostosis cranii the anatomical findings have consisted of new bone tissue in which calcification has taken place both in the surface layers and in the diploë, so that the latter is converted in some cases into a coral-like tissue; in others into a hard tissue like ivory, as was found in a case of my own. Actual softening does not seem to have been observed excepting in a case reported by Stack,[6] but I know of no case in which a histological examination was made, and, therefore, we can only surmise that, as in osteitis deformans, an absorptive process may have produced the sponge-like spaces in the hypertrophied diploë.[7]

Stack's case, which I have not included because it is not clear that it is not a complication of hyperostosis with osteomalacia, should be studied in this connection, for if softening of the long bones is not a complication the case is a transition between the two types we are considering. At the autopsy the skull was found to be enormously and almost uniformly thickened. All the cranial bones were affected, including those of the face. The cerebellar portion of the skull was very protuberant, dipping down toward the neck, and measured here in thickness almost three inches. The bones of the skull, on section, were for the most part softer than natural, but the appearance was not quite homogeneous. In parts there were masses of more compact tissue, and in others the rarefaction had proceeded to such an extent as to leave spaces of an eighth of an inch in diameter. The half skull without the lower jaw weighed seven pounds and a half. The lower jaw weighed one pound. The pelvis was very light, very soft, and much distorted; it was markedly generally contracted, scoliotic, funnel-shaped, and beaked. The femora were both bent and a little softer than natural. The tibiæ were also bent, and in some places the external compact layer was replaced by softened bone developed from the periosteum. There was no overgrowth in any bone apart from the head. It will be noticed that the rarefying process resembles in the description that of osteitis deformans.

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[1] Paris Thesis, 1893.

[2] Nouvelle Iconographie de la Salpêtrière, 1894, t. vii. 17.

[3] Trans. Clin. Soc., London, xviii. 273.

[4] Nouvelle Iconographie de la Salpêtrière, 1894, t. vii. 1.

[5] Rev. d'Orthopedie, May 1, 1897, viii. 164.

[6] Bristol M. C. J., 1900, xviii. 316-320.

[7] Four cases of Horsley's (Practitioner, 1893) reported under the title of leontiasis ossium ought not to be overlooked entirely. The hyperostosis was of the nature of a bone tumor, and was removed by operation. Histological examination of the removed bone in two showed the presence of a process which was both absorptive and osteoplastic.

Now, although in numerous histological examinations of the bones in osteitis deformans the findings have been similar to those described by Packard, Steele and Kirkbride, this would seem not to be the whole story, for more or less calcification may take place in the new bone tissue, so that patches of greater or less extent of ivory-like density occur.[1]

Not a few autopsy findings in which the formation of new bone with calcification is the chief process might be easily cited. The fact is, whether absorption predominates or new bone formation without calcification or with calcification, is probably either a matter of stage in the process or dependent on unknown determining factors. At any rate, as a matter of observation, one process may predominate in one bone and the other process in another in the same case. The autopsies, then, thus far made describe a combination of anatomical processes which may be briefly stated to be: (*a*) Absorption of bone; (*b*) new formation of bone tissue without calcification; (*c*) new formation of bone tissue with calcification. Any of these processes may predominate.

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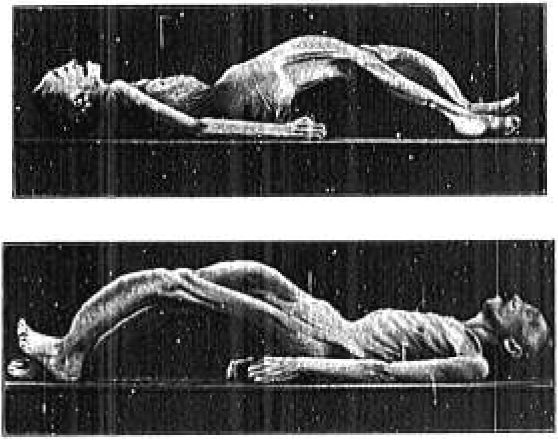
[1] Paget, in describing the findings in his first case, states that "the compact substance of the bones was in every part increased in thickness." "In the greater part of the walls the whole construction of the bone was altered into a hard, porous, or finely reticulated substance, like very fine coral. In some places, especially in the walls of the femur, there were small, ill-defined patches of pale, dense, and hard bone looking as solid as brick. In the compact covering of the articular ends of the long bones . . . the increase of thickness was due to encroachment on the cancellated texture, as if by filling its spaces with compact porous new-formed bone." Microscopic examination confirmed the macroscopic findings of new bone formation, with calcification. Bowlby describes similar changes in a femur, the only bone affected, remarking upon the formation of "new bone, sometimes of a hard, porcellanous appearance, and again of a more cancellous nature." Bowlby's case may be questioned as a true example, owing to only a single bone being affected, and yet the similarity of the changes to those found by Paget should be noted. Silcock, in an important observation, states that in a femur the superadded bone was everywhere compact and ivory-like excepting at one spot.

Lunn, again, while describing changes identical with those found by Packard, Steele and Kirkbride, also notes in addition the formation of calcified bone, which, as parallel lamellæ, reduced the size of the Haversian canals to the smallest calibre.

Equally important in showing calcification is the chemical analysis, which demonstrates substantially no deviation from the normal amount of lime salts in the bone (Paget) and even an increase (Robin, Gilles de la Tourette, and Magdalaine).

FIG. 5.



Sophia D., aged 73. Osteitis deformans. From a photograph kindly sent me by Mr. J. R. Lunn, F.R.C.S.

It is an interesting fact, to which attention has not been called in this connection, that in young, healthy growing bones an allied process takes place. The bone tissue around the Haversian canals may be absorbed, as in osteitis deformans, even to the extent of producing "irregularly bounded cavities of varying size with eroded edges, and lamellæ appearing as though gnawed away at points." Thus are formed the Haversian spaces. Reformation of new bone may then take place and fill up these spaces (Frey's *Histology*). This process is plainly a normal trophic one. This would suggest that it is within the bounds of possibility that the process in osteitis deformans is a modification or perversion of the same process which is provided for by nature in normal bones. Under such an hypothesis it would be a nutritive or trophic disorder.

In hyperostosis cranii it is possible that the anatomical process may be the same as in osteitis deformans, only that the process of calcification has predominated, and hence the greater density of the bones of those skulls examined in this disease as compared with the bones examined in osteitis deformans. But it must be borne in mind that very few cases of hyperostosis cranii observed during life have come to an autopsy, and of these none have been submitted to microscopic examination, and in none, unless Stack's can be accepted, have any of the long bones been examined either macroscopically or microscopically, so that, after all, we have no positive knowledge that the long bones have not to some degree participated in the process. Then, too, in Paget's disease very few bones in any one case have been histologically examined; but, as the facts stand, of the bones examined in the same case one or the other has shown considerable calcification, while another has shown less. The evidence thus far is too fragmentary

FIG. 6.

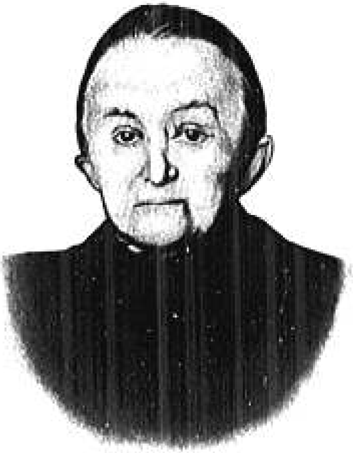


FIG. 7.

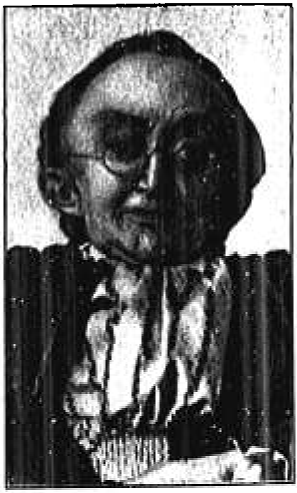


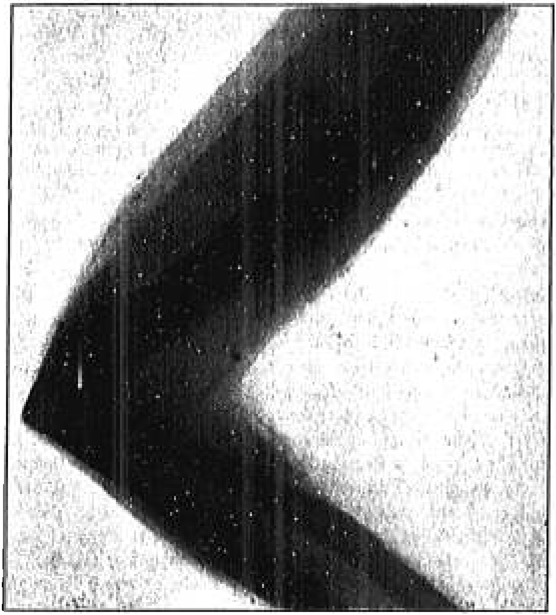
FIG. 6.—CASE III. Mrs. W., 1896. From Edes' article.

FIG. 7.—CASE III. Mrs. W., 1902. Osteitis deformans, formerly thought to be hyperostosis cranii. *Compare with Fig. 6, which is the same case photographed in 1896.*

to allow us to form a definite conclusion based on the anatomical findings alone.

CASE III.—Since the above was written I had an opportunity, through the kindness of Dr. Edes, to re-examine the case which he reported in 1896[1] under the title of hyperostosis cranii. I find that this case has developed into one of Paget's disease. Since 1896 the hypertrophic process in the head has greatly increased, as may be seen by comparing the photographs. (Figs. 6 and 7.) *Almost all, if not all, the long bones of the body are affected.* The right humerus is particularly deformed in a characteristic way, as is shown in the accompanying skiagram. (Fig. 8.) There is kyphosis in the lower dorsal region and deformity of the sternum. The clavicles have

FIG. 8.



CASE III. Osteitis deformans; right arm.

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[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, July, 1896.

escaped. The attitude of the patient is characteristic. What is of particular interest is that some of the phalanges of the fingers show traces of the disease in that they are bent, and the bones of the tarsus of one foot appear to be thickened. Then the nervous system shows certain abnormalities. There is general myasthenia, amounting to a paresis. The gait is paretic and unsteady, so that she requires help to maintain her balance in walking. She has a tendency to fall, not due to paresis, but no true ataxia can be made out, and Romberg's symptom is absent. The tactile and pain senses are normal; the knee-jerks are exaggerated. Plantar reflexes are absent. She has marked difficulty in swallowing, so that, for example, a glass of milk was drunk with great slowness and caution. The tongue protrudes straight; the face moves more to the right than to the left in speaking. The eyes are protruding, and there is a twitching of the right upper eyelid. There is decided deafness. There is no evidence of arterial atheroma, but there is an aortic systolic murmur. It is difficult to ascertain the exact time of development of the disease in the long bones. The patient says that her own attention was not called to these changes until after she had been observed by Dr. Edes, who tells me that he does not remember having made an examination of the limbs. It is possible, therefore, that the long bones may have been affected before 1896.

This case suggests the possibility that some of the other reported cases of hyperostosis cranii either may have developed later into Paget's disease, or that, if they had been more critically examined, the long bones would have been found to have been affected. As a matter of fact, in very few instances is any specific reference to the long bones made in the reports, and it is doubtful if they have been often examined. No reference to the long bones is made in Putnam's observations, and it is probable that they were not examined, as they were not in my own first case.

Osteo-arthritic Changes. The frequency with which osteo-arthritic changes are found in Paget's disease has not received the attention which they invite. These changes are identical in character with those found in certain types of rheumatoid arthritis, or, perhaps more correctly, osteo-arthritis. They are always regarded as evidences of coexisting rheumatoid arthritis rather than as different manifestations of the main pathological process. There are many facts which tend to show the incorrectness of this view.

In the first place, the frequency with which osteo-arthritic changes occur suggests some sort of kinship between this process and that in the body of the bones rather than the coincidence of two separate diseases.

Richard pointed out what he called transition cases between the two diseases. Humphrey calls particular attention to the presence of the two diseases in his specimens of a femur and tibia, as does Bowlby, who, in describing the appearance of the femur already referred to, specifically states that "some parts of the head and neck present changes exactly similar to those noted in an early stage of rheumatoid arthritis, the bone being smooth and porcellanous, with growth of nodosteophytes and with the worm-eaten appearance so common in this disease." In one of Stilling's cases von Recklinghausen found arthritis deformans at the autopsy. Goodhardt, in one case, describes deposits of new bone along the bodies of the vertebræ anteriorly, resembling in the description spondylitis deformans. In another case Goodhardt states that "bones of hard new-growth projected slightly from the substance of the bodies and welded the bones together by a tough, tuberculated mass, which looks not unlike the nodular masses found in some extreme cases of osteo-arthritis when that disease attacks the spine." Equally if not more remarkable findings in this particular, however, are those of Lunn, who describes a condition of the vertebræ exactly similar to that characteristic of spondylitis deformans of the type we are considering. "Projecting from the sides of some of the bodies of the vertebræ (chiefly lumbar) were well-marked bosses of new bone with disappearance of the intervertebral disks, and bony ankylosis had taken place at different intervals."[1]

The rigidity and ankylosis of the spine, which clinically is frequently observed in Paget's disease, undoubtedly is often, though not necessarily, due to a condition identical with that found by Goodhardt and Lunn, and described by Goldthwait in his monograph referred to. Clinically, also, ankylosis of the larger joints is not infrequently observed in Paget's disease, a process which is hard to explain by the absorptive and formative processes peculiar to osteitis deformans proper, and is probably due to the osteo-arthritic processes found at autopsies.

In my case nodosities are present in some of the phalangeal articulations, strongly suggestive of osteo-arthritis. In three of Lunn's cases ankylosis of the larger joints was present, and in a fourth there were bony growths about the knee-joints.

When we consider the variations in the anatomical processes found in osteitis deformans, there does not seem to be any good reason for regarding these osteo-arthritic changes as anything more than a predominance of the hypertrophic process which is observed in the bodies of the bones—a view which will receive support when we come to consider the disease as a trophic derangement.

In hyperostosis cranii, as well as in Paget's disease, the vertebræ sometimes take part in the hypertrophic process, or at least this seems to be the case from what can be made out during life. At any rate, fixation of the spine (my case) and thickening of the vertebræ can be felt (Starr).

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[1] Compare this with the following description of Goldthwait from his article on "Spondylitis Deformans, or the Spinal Form of Osteo-arthritis:" "Pathologically, the disease consists of a nodular enlargement of the edges of the articular cartilages, with the subsequent ossification of these nodes and an extension of the process into the ligaments which have their origin or insertion near by. With this hypertrophy at the edges of the cartilage the centres or areas of pressure usually undergo atrophy." . . . "As the process continues either the two surfaces of bone fuse or remain in apposition."

Special Pathology. Baumgarten, Starr, and Putnam have insisted that hyperostosis cranii is a trophic disorder, while several writers have done the same for Paget's disease. The thought suggests itself whether all the bone lesions commonly found associated in osteitis deformans and hyperostosis cranii, including those referred to rheumatoid arthritis, different as these anatomical lesions are, may not represent only perversions of a central trophic arrangement analogous to the so-called trophic lesions observed in spinal and nerve lesions. But when we attempt to point to any particular derangement, whether in the nervous system or elsewhere, we are made conscious of the blindness of our knowledge. And yet there are a number of facts which may have a bearing at least on the solution of the problem. So far as concerns the possibility of a central nervous derangement producing the osseous changes, the lesions in tabes and syringomyelia are instructive. In these diseases as well as some others affecting the central gray matter there is a very remarkable tendency to calcification or ossification of the ligaments and absorption of the cartilages of joints and development of bony masses about them—changes which in themselves have a very close resemblance at least to what occurs in osteoarthritis. Then, again, the process may be one of rarefaction or hypertrophy, and either may predominate. In the latter case the shaft of a long bone may undergo an extraordinary increase in size by the development of new osseous tissue on the surface. Further than this, deformities of the skull occur in syringomyelia, characterized by bossing of the frontal and parietal eminences and prominence of the forehead.

A very remarkable case was published by Hale White,[1] under the title of "Hyperostosis Cranii." Later the case came to autopsy as the result of operation for fits, and was described by Collier. Unexpectedly a condition of syringomyelia[2] was found, which did not give rise to the ordinary sensory symptoms of that disease, although there was a spastic atrophic paralysis of one arm of obscure origin, but thought before death to be cerebral. The skull was very remarkable. The deformity which had been taken for a hyperostosis was a projecting ridge or fold extending from the temporal region on each side backward around the occiput and overhanging the neck. It was as if the spine and base had been telescoped into the skull, which overhung the base like a mushroom.

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[1] British Medical Journal, 1896, vi. 1377.

[2] Lancet, January 5, 1901. The cavity extended from the left inferior olivary downward in the posterior horn to the sixth dorsal, excepting that it intermitted from 8 c. to D 4; marked old degeneration in the right pyramid (tract?), which could be traced to lumbar region. Nerve cells normal by Nissl method; brain normal. Report too incomplete to allow cause of arm paralysis to be determined.

The bones of the skull were for the most part small, and in some places thin, but in other places they were "unduly large" (hypertrophied?). The deformity had begun in childhood, and was supposed to have followed a fall upon the head.

The nature of the bone changes is not clear, but it was apparently one of perverted nutrition, and very likely connected with the syringomyelia as one of the trophic lesions of that disease.

The combined anatomical picture presented by these lesions in nervous diseases is very different, of course, from that seen in Paget's disease, but the individual processes suggest the variety of changes which may be brought about by one and the same nervous derangement. Several writers have suggested that the *fons et origo* of Paget's disease was to be found in the nervous system. Stilling, in 1889, attributed the coexistence of the two diseases to coincidence, and this view has been repeated successively by later writers. The possible dependence of osteitis deformans upon some kind of nervous lesion, it seems to me, has been rather hastily discarded without due consideration of the facts, and perhaps without a critical examination of the original records. Sometimes it has been taken for granted that the autopsy findings have negatived such an hypothesis. One of the later monographs states that "the results of many examinations . . . have shown the cord and bone nerves . . . to be perfectly normal." . . . This seems to be a hardly well-considered statement. I have not been able to find that the spinal cord has been examined at all, excepting in ten cases, and in five of these there was more or less evidence of pathological changes. In three (Gilles de la Tourette and Marinesco two, Levi one) a gross lesion in the form of posterior sclerosis was found under the microscope. In one, that of Pic, the spinal cord, to the naked eye, showed a grayish tint in the two posterior columns and in the right pyramidal tract. In one case (Stilling) some, though not marked, changes were found by von Recklinghausen, viz.: There was a small gliomatous growth in the cervical region and sclerosis of the ependyma. To the naked eye the gray substance throughout the whole length of the cord was white, opaque, and not easily distinguishable. The import of this is not mentioned by the reporter, but the ganglion cells and nerve trunks under the microscope appeared to be normal. It is suggestive that this case exhibited contractures and muscular weakness, if not paralysis, which must have been of spinal origin. In the sixth case, that of Lunn,[1] the spinal cord was found to be "soft in the cervical region, almost pulpy opposite the first and second dorsal and seventh cervical vertebræ."

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[1] Transactions of the Clinical Society, vol. xviii.

"A year before the patient died he developed symptoms of bulbar paralysis, with extreme wasting of the tongue, dysphagia, and some loss of taste." *No microscopic examination was made.* It was evident that the cord softening, from its situation, was something in addition to the bulbar disease.

This leaves four cases to be accounted for. In two of these four (Stilling, Noizard, and Bourges) there was no microscopic examination of cord or nerves at all; but in the remaining cases, two, the microscopic examination showed the cord and nerves to be normal. Of ten cases, then, there was more or less good evidence of disease in six, not examined microscopically in two, and normal in two only. It does not appear that in either of the normal cases (Stilling and Goodhardt) any of the finer methods of technique were employed, including the special stains. One was examined as far back as 1878 (Goodhardt). The report of this simply states that "the spinal cord was quite healthy, both to the eye and under the microscope." The nerves were not examined. We must also bear in mind that we do not know what cells or elements in the cord, if any, regulate the nutrition of the bones, so that we do not even know where to look for the lesions which may be responsible for bone and arthritic changes. Therefore, it may well be easy to overlook them, as, indeed, the history of many originally obscure nervous diseases shows. At any rate, from this examination of the reports of autopsies it would appear that the frequency with which changes have been found in the nervous system has been overlooked. More opposed to the nervous origin of the disease is the fact of entire absence of nervous symptoms in the mass of cases; but this objection, it seems to me, is based on a too superficial view of the question. In the first place, as I have said, we know almost nothing of the seat of the trophic functions of the cord beyond the fact that lesions of the anterior cornua lead to muscular atrophy, and we are entirely ignorant of what elements in the cord subserve nutrition of bone or skin and other organs. Even in tabes we are ignorant of the special lesion which causes the trophic changes in the bones, whether seated in the anterior or posterior portions or in the peripheral nerves. *It is not inconceivable that as degeneration of the anterior cornua may cause myopathies without other symptoms, so lesions of other special cell groups may cause osteopathies without other spinal symptoms.* In the second place, it is a curious but interesting fact that in neither of the two cases of Gilles de la Tourette nor in that of Levi, in all of which an extensive sclerosis was found, were there any recognizable nervous symptoms during life, not even absence of knee-jerks, excepting that in Levi's case there was diminution of intelligence, ready weeping, and binocular nystagmus, and at the end only incontinence of urine and feces.

But it is exceedingly improbable that the lesion, if it is to be found in the nervous system, is that of one of the stock nervous diseases. If such were the case we should expect to find the bone lesions occurring from time to time as manifestations of one or more of these diseases. It is much more probable that the pathological changes may be of a more general and finer type, such as would interfere with nutrition alone. Perhaps the arterial sclerosis which almost always is found, and which sometimes is so extraordinarily obtrusive in the younger cases, may be the primary source of nutritional changes. In the first of Gilles de la Tourette and Marinesco's cases the sclerosis of the posterior columns did not extend below the dorsal cord (the cervical cord was overlooked), and some of the fibres in the lateral columns were diseased. (The nerves were not examined.) In the second case, beside the sclerosis of the posterior columns most developed in the dorsal region, the peripheral nerves were the seat of an interstitial neuritis. The authors do not consider that the disease in the cord was a true posterior sclerosis, but rather an atrophy of nerve fibres. Levi also insists that the extensive sclerotic changes, with disappearance of myeline fibres, that he found in both posterior and lateral columns and other regions were to be regarded as a pseudosystemic sclerosis of vascular origin. The vessels throughout were the seat of a periarteritis and endarteritis. The spinal nerves showed irregular thickening of their connective tissues; the sciatic showed practically the same changes that were found in the cord.

It would seem to be highly possible that as a result, not of a posterior sclerosis or a lateral sclerosis, but of the vascular sclerotic changes that are always or almost always found in osteitis deformans, nutritional impairment might be brought about in the central nervous arrangements which we have to suppose govern the nutrition of the bones, just as the anterior cornua govern the muscles, and that future researches may reveal the nature and seat of these changes. In emphasizing this hypothesis I do not overlook the fact that in old people changes in the nervous system are apt to develop, and that the occurrence of these changes with bone lesions may be a coincidence.

What I have said is mostly speculative, but, considering the absolute blindness of our knowledge of osteitis deformans and the completely negative position in which this subject has been left by all writers on the subject, I have thought it might not be without value to put together the allied facts in our possession, hoping that they might furnish a working hypothesis and point the way for further pathological investigation, by which alone we can understand this most remarkable disease.

By way of summary, then, I would say:

1. We have no sure ground for differentiating hyperostosis cranii from osteitis deformans.

2. Hyperostosis cranii and osteitis deformans are probably trophic disorders.
3. Various clinical and pathological facts seem to indicate that they are at least allied disorders, and perhaps only different manifestations of one and the same disease.
4. The osteo-arthritic changes so commonly found in osteitis deformans are probably manifestations of the disease, and not complications.
5. The results of autopsies thus far made do not at all exclude the nervous system as the seat of the trophic derangement, but the changes that have been found in the spinal cord and peripheral nerves and analogy with other known lesions like those of tabes and syringomyelia suggest a neuropathic origin similar to that of the myopathies.
6. In future cases the nervous system should be exhaustively studied.

[NOTE.—I wish to express my obligation to Dr. Packard for his great kindness in loaning me his references to the literature and abstracts of reported cases, thus materially aiding this study.]

CERTAIN CHARACTERISTICS OF OSTEITIS DEFORMANS.

BY REGINALD H. FITZ, M.D.,
OF BOSTON.

THE first case reported by Dr. Prince subsequently came under my care at the Massachusetts General Hospital, having been referred to me by Dr. M. A. Morris, of Boston. There are certain points of interest resulting from my study of the patient and the disease concerned which I desire to place on record, even at the risk of duplicating some of the observations which Dr. Prince may have made.

These concern especially the recognition, by means of the Röntgen rays, of the alterations of the bones and the intimacy of the relation between cranial hyperostosis and osteitis deformans.

In this connection I wish to acknowledge my indebtedness to Mr. Walter Dodd, of the hospital, for the photographs and skiagraphs which will illustrate my remarks, and especially for his expert assistance in the interpretation of doubtful points in the latter series of pictures and in establishing the conclusions to be drawn from them. I am indebted also to my assistant, Dr. R. F. Gibson, for his aid in obtaining the completest possible record of the case, which is offered as a supplement to that of Dr. Prince.

The patient was born in Boston, in and near which she has always lived. Entered the Massachusetts General Hospital February 6, 1902. Her father died of phthisis, aged eighty-four years; her mother died